

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-33 are pending in this application.

Claims 1-6, 18-20 and 26-33 were examined on the merits and stand rejected.

Claims 7-17 and 21-25 were withdrawn as non-elected subject matter.

Applicants again request the consideration and examination of additional species in accordance with U.S. election of species practice, upon an indication of allowance of the generic claims and elected species.

Claims ~~1 and 18~~ have been amended to better conform to U.S. practice. These claims have also been amended to specify that the "analyte" has a molecular weight of less than 5000, as supported by the disclosure, for example, at page 7, lines 30-31.

Claims 26-31 were objected as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all limitations of the base claim and any intervening claims. Applicants appreciate the Office's indication of allowable subject matter. Claims 26 and 27 have been amended to independent form as suggested. Thus, claims 26

and 27 and all claims dependent thereon (i.e., claims 28-31) should now be in condition for allowance.

No new matter has been added by the above claim amendments.

The specification has been amended at page 13 to capitalize the trademark term "SEPHAROSE". No new matter has been added by this amendment.

Applicants are submitting the present amendment without prejudice to the subsequent prosecution of claims in some or all of the subject matter which might be disclaimed by virtue of this response (although none is believed to be), and explicitly reserve the right to pursue some or all of such subject matter, in divisional or continuation applications.

Applicants thank the Examiner for the careful examination of this case and respectfully request reexamination and reconsideration of the case, as amended. Below Applicants address the rejections of the Office Action and explain why the rejections are not applicable to the pending claims as amended.

II. OBJECTIONS TO THE SPECIFICATION & CLAIMS

The specification was objected to for the improper use of trademarks for the reasons noted in item 6 on page 3 of the Office Action. Claim 6 was objected to for the same reasons. See item 7 on page 3 of the Office Action.

These rejections are respectfully traversed.

SEPHAROSE is indeed a registered trademark. Accordingly, Applicants have amended page 13 of the specification to capitalize "SEPHAROSE".

However, it is believed that "cocaine" and "morphine" are not. Instead, these terms are mere trivial chemical names, as evidenced from the Merck Index 2006. Applicants have included a copy of the relevant pages thereof. Thus, Applicants see no need to amend either the specification or the claims with respect to the term "cocaine" and "morphine" as they are not believed to be trademarks.

Therefore, withdrawal of the above objections is solicited.

III. INDEFINITENESS REJECTIONS

Claims 1-6, 18-20, and 26-33 were rejected under 35 USC §112, second paragraph, as being indefinite for the reasons set forth in Items 8A-8B on page 4 of the Office Action.

This rejection is respectfully traversed for the following reasons.

In item 8A, the Office argues that the term "small analyte" in claims 1 and 18 is indefinite. In reply, Applicants have amended independent claims 1 and 18 to specify that the small analyte has a molecular weight of less than 5000. Support can be found in the disclosure, for example, at page 7, lines 25-31 of the PCT publication. At this location, the specification

refers to the term "small analyte" as low molecular weight analytes that generally have molecular weights of less than 5000. Accordingly, the amended language clearly defines what is meant by the term "small analytes." Thus, Applicants respectfully submit that such language would be clear and definite to the skilled artisan.

In item 8B, the Office argues that the recitation "wherein the second binding partner is obtained from a naive display..." in claims 1 and 18 is indefinite. The Office suggests amending the claims to recite a structural component to give weight thereto. Applicants respectfully disagree.

The claimed immunoassay and method is directed to a non-competitive immunoassay for small analytes, wherein the analyte is first bound to a first binding partner, and then to a second binding partner that binds to the complex of the analyte and the first binding partner. The second binding partner is obtained using a naive display recombinant binding partner library.

Non-competitive immunoassays have many advantages over competitive immunoassays, such as improved speed, sensitivity and specificity. A non-competitive immunoassay is based on the use of two antibodies that bind to two different epitopes of the antigen. This works well for high molecular weight analytes, but when the analyte is small (as in the instant claims), there is not enough space for binding the two different antibodies. Still

there are some publications that disclose non-competitive assays for small analytes. In these assays a secondary anti-immune complex (anti-IC) antibody is used, which binds to the immune complex formed by the primary anti-analyte antibody and the antigen, but not to the analyte or the primary antibody alone. The difficulties here lay in obtaining the appropriate secondary anti-IC antibody. The immune complex used for immunization tends to break down before the response to the immune complex is obtained.

The present invention overcomes this problem. Specifically, in the last paragraph starting at the bottom of page 2 of the specification, it is stated that the present invention provides an immunoassay, which circumvents immunization of animals with an immune complex (IC), which is extremely difficult. At page 3, lines 6-9, it is further indicated that the difficulties associated with raising anti-IC antibodies can be avoided by providing the necessary anti-IC antibodies from a display recombinant binding partner library, instead of from immunized animals. Thus, the point of such is that the desired second binding partner of the claims is obtained from a non-immunized source. In other words, the desired second binding partner is obtained from a naive binding partner library as set forth at page 8, line 24 and as illustrated in Example 1 at page 14. It is noted that claims 1 and 18 have been amended to better reflect this feature.

The use of a naive recombinant binding partner library provides a complete solution to the problem associated with immunizing with an immune complex. Therefore the suggested amendment of structural limitations is unnecessary for unambiguously solving the technical problem recognized from the application. Further, possible display libraries are known in the art, and set forth in the first paragraph at page 6 of the application. Binding partners are set forth in the first paragraph at page 5 under the title Detailed Description of the Invention, where it can be seen that the binding partners usually are proteins such as antibodies or antibody fragments, preferably fragments comprising the ligand-binding site, such as Fab, or scFv. It is the use of a naive recombinant binding partner library, not the type of display library, nor the type of antibody fragment involved that is essential for avoiding the need to immunize with an immune complex.

Based on such, it is respectfully submitted that the amended claims are thus clear, definite and have the full antecedent basis.

Therefore, the above-noted indefiniteness rejections are believed to be overcome, and withdrawal thereof is respectfully requested.

IV. WRITTEN DESCRIPTION REJECTION

Claim 2 was rejected under 35 USC § 112, first paragraph, on the basis the specification allegedly fails to comply with the written description requirement for the reasons set forth in item 9 on pages 5-7 of the Office Action.

Applicants respectfully traverse this rejection.

The test for sufficiency of written description is whether the disclosure reasonably conveys to the skilled artisan that the inventor had possession at the time of filing of the subject matter which is claimed. M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2163, I, 2100-159, 1st column, 2nd paragraph.

This test may be satisfied by: (1) a reduction to practice; (2) a reduction to drawings/chemical formulas; (3) a disclosure of relevant identifying characteristics, such as structure or other physical and/or chemical properties, to sufficiently describe the claimed invention in full, clear, concise and exact terms; (4) a disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure; (5) a sufficient description of a representative number of species; or (6) a combination of the above, sufficient to show the inventors were in possession of the invention. M.P.E.P. (Eighth Ed., Rev. 6 (September 2007) at §2163,II, A, 3a(i)-(ii).

According to the Official Action, the written description is not commensurate in scope with the claims drawn to the utility of any and all fragment, fragment antibody, and single chain fragments. In this connection, Applicants again wish to emphasize that the key of the claimed invention resides in the use of a naive binding partner library, and not in the type of binding partner used in said library.

Further, it should be noted that the antibody fragments set forth in the present claim 2 (Fab and scFv) are well defined parts of immunoglobulines generally known in the art. As such, antibody fragments Fab and scFv are well known and characterized parts of immunoglobuline antibodies. This will clearly be recognized by those skilled in the art. Further, the specification describes in detail how to obtain and use certain Fab fragments and scFv fragments. See, for instance, the discussion at page 13, lines 8-34, and at page 14, lines 5-28, wherein the use of M1 Fab fragments are discussed. At the same location and at further places in the disclosure (for instance at page 14, line 3 to page 15, line 25), the specification discusses how to obtain and use the scFv fragment K11.

Further, the Office even acknowledges that the specification discloses how to use antibody fragments, i.e., antibody sequences consisting of SEQ ID No. 1 through SEQ ID No. 5.

It is respectfully submitted that such disclosure constitutes, at least 1) a reduction to practice for the use of various Fab and scFv antibody fragments; and 2) a disclosure of relevant identifying characteristics, such as structure or other physical and/or chemical properties, to sufficiently describe the claimed invention in full, clear, concise and exact terms, to show that Applicants were in the possession of antibody fragments, Fab and scFv, at the time of filing. Moreover, the numerous examples of peptide sequences SEQ ID NOs. 1-5, as discussed above, and in the specification constitute a reduction to practice of a sufficient number of a representative species to show the inventors were in possession of the claimed invention. Accordingly, the skilled artisan, upon reading the disclosure and in view of the knowledge in the art, could readily construct and use various antibody fragments Fab and scFv from various antibodies based on the guidance in the disclosure and the knowledge in the art. Thus, the specification provides full written support for the claimed use of antibody fragments Fab and scFv.

Therefore, it is respectfully submitted that the skilled artisan would reasonably believe that Applicants were in possession of the claimed subject matter at the time of filing of the application. For this reason, the above written description rejection is believed to be untenable and should be withdrawn.

V. PRIOR ART REJECTIONS

YOKOZEKI

Claims 1-4, 18-20, and 33 were rejected under 35 USC § 102(a) as allegedly anticipated by YOKOZEKI (Analytical Chemistry A-E, 2002, Vol. 74, pages 2500-2504) for the reasons set forth in Item 10 on page 7 of the Office Action.

This rejection is respectfully traversed.

It is well established that to anticipate a claim, the cited prior art reference must disclose or suggest each and every element of the claimed invention. See, M.P.E.P., 8th Ed., Revision 6 (September 2007) at Section 2131.

Independent claims 1 and 18 recite "first binding partner that binds to said analyte, and a second binding partner that binds to the complex of said analyte and said first binding partner." Applicants respectfully submit that YOKOZEKI fails to disclose or suggest this feature of the independent claims.

YOKOZEKI discloses a homogenous non-competitive immunoassay for the detection of small haptens based on the antigen-dependent reassociation of antibody variable-domains and beta-galactosidase. As binding partners, a pair of an antibody VH region fragment and its VL region fragment are used fused to C- or N-truncated beta-galactosidase. The VH and VL fragments in YOKOZEKI recognize one and the same antigen (NP). By contrast, the binding partners used in the present claims recognize different molecules. In other words, in the present claims, the

first binding partner binds to the analyte, and the second binding partner specifically binds to the immunocomplex formed between the first binding partner and the analyte. Based on this difference, it is clear that the claims are not anticipated by YOKOZEKI.

Therefore, Applicants respectfully submit that YOKOZEKI fails to anticipate claim 1 and claims dependent thereon the claimed invention, as the reference fails to disclose each and every element thereof.

For this reason, the above 102(a) anticipation rejection over YOKOZEKI is untenable and should be withdrawn.

YOKOZEKI in view of CHAN

Claims 5, 6 and 32 were rejected under 35 USC § 103(a) as allegedly obvious over YOKOZEKI in view of CHAN (Cytometry, Vol. 44, pages 361-368, 2001) for the reasons set forth in item 11 on pages 8-9 of the Office Action.

This rejection is respectfully traversed.

The above arguments with respect to YOKOZEKI are reiterated herein.

Furthermore, YOKOZEKI is said to differ from the instant invention in not specifically teaching the detection of drugs of abuse. In this respect, Applicants refer to the comments above, in which is noted that YOKOZEKI uses a pair of antibody fragments that recognize the same molecule, whereas the invention of the claims uses a pair of binding partners, one of

which recognizes an analyte, and the other the immunocomplex between the analyte and the first binding partner.

CHAN discloses a new method for FRET using spectral variants of green fluorescent protein (GFP). Still a combination of the teachings of YOKOZEKI with those of CHAN would not lead the invention of the claims, because the binding partner reagents of YOKOZEKI recognize the same molecule, whereas those of the present claims do not.

Therefore, Applicants respectfully submit that YOKOZEKI, taken alone or in combination with CHAN, fails to teach, suggest or make obvious each and every element of claims 5, 6 and 32.

For this reason, the above 103(a) obviousness rejection over YOKOZEKI and CHAN is untenable and should be withdrawn.

VI. ALLOWABLE SUBJECT MATTER

Claims 26-31 were objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims.

Applicants again thank the Examiner for the indication of allowable subject matter. Claims 26 and 27 have been amended to independent form as suggested. Claims 28-31 depend thereon. Therefore, claims 26-31 should now be in condition for allowance.

VII. CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and an early notice to that effect is respectfully requested.


If the Examiner has any comments or proposals for expediting prosecutions, please contact the undersigned attorney at the telephone number below.

Please charge the requisite fee of \$420 for the two extra independent claims added herewith, to our credit card as set forth in the attached Credit Card Payment Form.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following item(s):

- The Merck Index 2006, pages 6276, 2452.